

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing:

15 March 2001 (15.03.01)

International application No.:

PCT/US00/24714

Applicant's or agent's file reference:

7772/JB

International filing date:

08 September 2000 (08.09.00)

Priority date:

10 September 1999 (10.09.99)

Applicant:

UNDERINER, Todd, Laurence et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International preliminary Examining Authority on:

02 January 2001 (02.01.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 7772/JB	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 24714	International filing date (day/month/year) 08/09/2000	(Earliest) Priority Date (day/month/year) 10/09/1999
Applicant THE PROCTER & GAMBLE COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/24714

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/48 A61K7/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	US 6 066 673 A (UNDERINER TODD LAURENCE ET AL) 23 May 2000 (2000-05-23) column 1; claims	1
A	EP 0 542 371 A (STERLING WINTHROP INC) 19 May 1993 (1993-05-19) abstract claim 1	1
A	EP 0 594 257 A (STERLING WINTHROP INC) 27 April 1994 (1994-04-27) claims 1,14	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

30 January 2001

Date of mailing of the international search report

05/02/2001

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Authorized officer

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/24714

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6066673	A	23-05-2000	AU 2903799 A	27-09-1999
			EP 1062264 A	27-12-2000
			NO 20004550 A	10-11-2000
			WO 9946316 A	16-09-1999
EP 0542371	A	19-05-1993	AU 656027 B	19-01-1995
			AU 2605792 A	20-05-1993
			CA 2082774 A	16-05-1993
			CZ 9203388 A	16-06-1993
			FI 925166 A	16-05-1993
			HU 65694 A	28-07-1994
			HU 9500612 A	28-11-1995
			IL 103747 A	15-06-1998
			JP 6122675 A	06-05-1994
			MX 9206568 A	01-05-1993
			NO 302887 B	04-05-1998
			NZ 245126 A	26-01-1996
			RU 2114835 C	10-07-1998
			SG 52778 A	28-09-1998
			US 5380737 A	10-01-1995
			US 5464852 A	07-11-1995
			US 5578623 A	26-11-1996
			US 5773456 A	30-06-1998
EP 0594257	A	27-04-1994	US 5306818 A	26-04-1994
			AT 140227 T	15-07-1996
			AU 679446 B	03-07-1997
			AU 4452693 A	05-05-1994
			CA 2105731 A	24-04-1994
			CZ 9302210 A	18-05-1994
			DE 69303573 D	14-08-1996
			DE 69303573 T	27-02-1997
			DK 594257 T	11-11-1996
			ES 2092751 T	01-12-1996
			FI 934675 A	24-04-1994
			GR 3021300 T	31-01-1997
			HU 68879 A	28-08-1995
			IL 107315 A	12-03-1999
			JP 6211849 A	02-08-1994
			MX 9305196 A	31-05-1994
			NO 933817 A	25-04-1994
			NZ 248360 A	28-08-1995
			SG 50627 A	20-07-1998
			SK 116693 A	08-02-1995
			US 5512589 A	30-04-1996
			US 5597841 A	28-01-1997

PATENT COOPERATION TREATY

PCT

REC'D 08 OCT 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference 7772/JB	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/24714	International filing date (day/month/year) 08/09/2000	Priority date (day/month/year) 10/09/1999
International Patent Classification (IPC) or national classification and IPC A61K7/48		
Applicant THE PROCTER & GAMBLE COMPANY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 02/01/2001	Date of completion of this report 04.10.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Ortega Plaza, M.D. Telephone No. +49 89 2399 8284 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/24714

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-33 as originally filed

Claims, No.:

1-18 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/24714

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-18.

because:

- ☒ the said international application, or the said claims Nos. 17,18 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-18 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

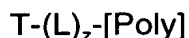
- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The requirements of clarity of the claims set forth in Article 6 PCT apply to each individual claim and to the claims taken as a whole. The present set of claims has been so unclearly worded that no opinion can be given with respect of the novelty and inventive step of the subject-matter claimed. The reasons are as follows:

Claim 1 relates to a "polymer conjugate having the formula



wherein T is a saccharin ring-comprising enzyme inhibitor component, L is a linking unit, [Poly] is a polymer component, z is 0 or 1."

The subject-matter of claim 1 lacks clarity. Moreover, an undue burden is put on the skilled reader, when construing the subject-matter of the said claim, since the claim encompasses such a large number of possibilities, that it is unlikely that all encompassed possibilities may be made or performed or solve the technical problem.

As above mentioned, claim 1 relates to a polymer conjugate, wherein the structural constituents have been defined by their function ("linking unit", "polymer component") or by the result-to-be-achieved ("enzyme inhibitor component"). These expressions cannot serve for defining without ambiguity the contribution to the art, since none of these terms has a clear technical meaning.

Additionally, the compounds of claim 2, which is dependent on claim 1, are not encompassed by claim 1. The reasons are i.a. that the formulae depicted in claim 2 do not fall within the generic formula depicted in claim 1. In particular, L may be absent or present one time in the compounds of claim 1 (see $(L)_z$, wherein z is 0 or 1), whereas in the compounds of claim 2 may contain L 1 to 100 times (see $[-(L)_z-]_i$, wherein i is 1 to 100).

Moreover, claim 2 lacks clarity, since it relates to a compound according to claim 1 "having a saccharin inhibitor **compon nt** of the formula", followed by two

formulae which represent a polymer conjugate and not a partial moiety. Moreover, it is unclear to which of the moieties and groups corresponds the list of options beginning with a) and ending with p). The use of the expression "mixtures thereof" as option p) together with its repetition in several of the other options is unusual in the context of defining radicals and groups present in a chemical structure as pool of options, and chemically misleading. Furthermore, option o) is chemically absurd, since the group R is linked to a carbon atom of a phenyl moiety it cannot be that two "R units" are linked to the same carbon atom. The expression "carbonyl unit equivalent" lacks clarity, since the conditions for the equivalency are unclear (chemical?, biological?, ...). The expression "polymeric unit" without further specification to its chemical structure and/or molecular weight, is unclear. It is unclear whether this is intended to include monomeric units and which is its the chemical nature or its size.

The above analysis applies mutatis mutandis to the dependent claims 3-13. Additionally, the compound depicted in claim 9 (dependent on claim 2) possesses two substituents in the aromatic ring which is in contradiction with the formulae depicted in claim 2. Hence claim 9 is not encompassed by claim 2. The above analysis applies mutatis mutandis to the composition claims 14, 15 and 16 and to the method claims 17, 18 insofar as they are characterized by the presence or use of the conjugates of claims 1 or 2. Additionally, the expression "for inhibiting enzymes" in claim 13 has no limitative character. It relates to a result-to-be-achieved which is identical to the problem to be solved. Moreover, since it may be any enzyme and in under any conditions (undefined) it may set unclear limits to the scope claimed. Claim 14 cannot be considered as "first-medical-use claim" since it is not stated that it should be a pharmaceutical composition and because there is no medical effect or use specified in that claim. The expression "for application to the human skin" has no other meaning than it is suitable for being applied to the human skin but has no clear technical meaning. Claim 16 is not a "first-medical use claim" for analogous reasons to that given for claim 13.

The method claim 18 has been worded as dependent on claim 16, which is a claim of product category, "composition".

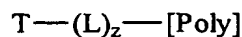
**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/24714

Finally, claims 17-18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT). The method for preventing human skin irritation according to claim 17 encompasses methods of therapeutical treatment of the human or animal body.

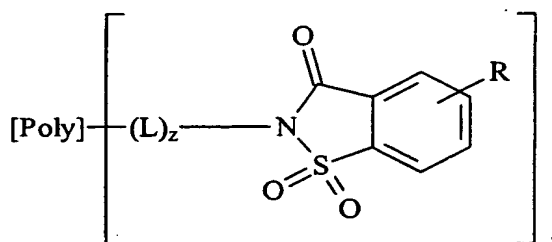
WHAT IS CLAIMED IS:

1. A polymer conjugate having the formula:



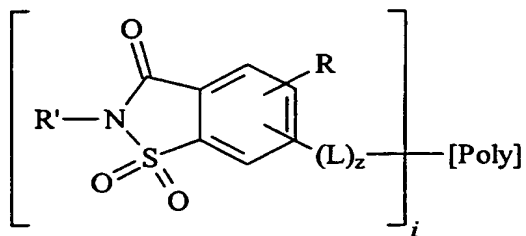
- 5 wherein T is a saccharin ring-comprising enzyme inhibitor component, L is a linking unit, [Poly] is a polymer component, z is 0 or 1.

2. A compound according to Claim 1 having a saccharin inhibitor component of the formula:

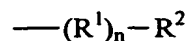


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or the formula:



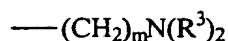
- a) hydrogen;
 b) C₁-C₁₈ substituted or unsubstituted, linear or branched alkyl;
 15 c) C₃-C₁₈ substituted or unsubstituted, linear or branched cycloalkyl
 d) C₂-C₁₈ substituted or unsubstituted, linear or branched alkenyl;
 e) C₂-C₁₈ substituted or unsubstituted, linear or branched alkynyl;
 f) C₆-C₁₈ substituted or unsubstituted aryl;
 g) C₂-C₁₈ substituted or unsubstituted heterocyclic alkyl;
 20 h) C₃-C₁₈ substituted or unsubstituted heterocyclic alkenyl;
 i) alkylenearyl having the formula:



25

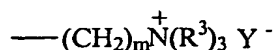
wherein R¹ is C₁-C₁₂ linear or branched alkylene, C₂-C₁₂ linear or branched alkenylene, or mixtures thereof; R² C₆-C₁₈ substituted or unsubstituted aryl, or mixtures thereof; n is from 1 to 16;

- j) an amino unit having the formula:



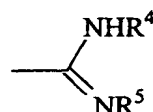
wherein each R^3 is independently C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl; m is from 0 to 10;

- k) a quaternary ammonium unit having the formula:



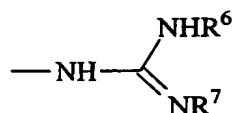
wherein each R^3 is independently C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl; Y is an anion of sufficient charge to provide electronic neutrality; m is from 0 to 10;

- l) a unit having the formula:



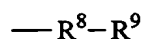
wherein R^4 is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^5 is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^4 and R^5 can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

- m) a unit having the formula:



wherein R^6 is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^7 is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^6 and R^7 can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

- n) a unit having the formula:



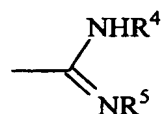
wherein R^8 is:

- i) $-(CH_2)_p-$, wherein p is from 0 to 12;
- ii) $-C(O)-$;
- iii) $-C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- iv) $-C(X)R^{11}C(X)-$, wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- v) $-C(X)NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;

- 5
- vi) $-C(X)NR^{10}R^{11}NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- vii) $-NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- viii) $-NR^{10}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 10 ix) $-NR^{10}C(X)R^{11}NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 15 x) $-NR^{10}R^{11}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 20 xi) $-NR^{10}C(X)R^{11}C(X)O-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xii) $-OC(X)R^{11}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 25 xiii) $-NR^{10}C(X)NR^{10}R^{11}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 30 xiv) $-R^{11}NR^{10}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; wherein X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xv) $-R^{11}NR^{10}C(X)NR^{10}R^{11}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or

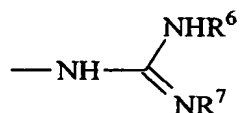
- unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR¹⁰, and mixtures thereof;
- xvi) -NR¹⁰-, wherein R¹⁰ is hydrogen, C₁-C₄ alkyl, or mixtures thereof;
- xvii) -O-;
- 5 xviii) -(R¹¹)_tC(X)(R¹¹)_t-; wherein R¹¹ is C₁-C₁₂ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1; X is oxygen, sulfur, NR¹⁰, and mixtures thereof;
- xix) -(R¹¹)_tOC(O)(R¹¹)_t-; wherein R¹¹ is C₁-C₁₂ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- 10 xx) -(R¹¹)_tC(O)O(R¹¹)_t-; wherein R¹¹ is C₁-C₁₂ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxi) alkyleneoxyalkylene having the formula:
- $$\text{---(R}^{12}\text{O)}_q\text{R}^{13}\text{---}$$
- wherein R¹² is C₂-C₆ linear or branched alkylene, substituted or unsubstituted phenylene; R¹³ is -(CH₂)_p-, wherein p is from 0 to 12; q is from 1 to 4;
- 15 xxii) -S-;
- xxiii) -(R¹¹)_tS(R¹¹)_t-; wherein R¹¹ is C₁-C₁₂ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- 20 xxiv) -(R¹¹)_tS(O)(R¹¹)_t-; wherein R¹¹ is C₁-C₁₂ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxv) -(R¹¹)_tSO₂(R¹¹)_t-; wherein R¹¹ is C₁-C₁₂ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxvi) or mixtures thereof;
- 25 R⁹ is:
- i) hydrogen;
- ii) C₁-C₁₈ substituted or unsubstituted, linear or branched alkyl;
- iii) C₃-C₁₈ substituted or unsubstituted, linear or branched cycloalkyl;
- iv) C₂-C₁₈ substituted or unsubstituted, linear or branched alkenyl;
- 30 v) C₂-C₁₈ substituted or unsubstituted, linear or branched alkynyl;
- vi) C₆-C₁₈ substituted or unsubstituted aryl;
- vii) C₂-C₁₈ substituted or unsubstituted heterocyclic alkyl;
- viii) C₃-C₁₈ substituted or unsubstituted heterocyclic alkenyl;
- ix) -OH;
- 35 x) -SO₃M;

- xi) $-\text{OSO}_3\text{M}$;
- xii) $-\text{NO}_2$;
- xiii) halogen selected from fluorine, chlorine, bromine, iodine, or mixtures thereof;
- 5 xiv) $-\text{C}(\text{Hal})_3$, wherein each Hal is fluorine, chlorine, bromine, iodine, or mixtures thereof;
- xv) $-\text{COR}^{14}$; wherein R^{14} is hydrogen, $-\text{OH}$, $\text{C}_1\text{-C}_{12}$ alkyl, $\text{C}_1\text{-C}_{12}$ alkoxy, or mixtures thereof; $-\text{N}(\text{R}^{15})_2$, or mixtures thereof; each R^{15} is independently hydrogen, $-\text{OH}$, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof;
- 10 xvi) $-\text{CH}(\text{OR}^{14})_2$ wherein R^{14} is hydrogen, $\text{C}_1\text{-C}_{12}$ alkyl, or two R^{14} units can be taken together to form a ring having from 3 to 5 carbon atoms; or mixtures thereof;
- xvii) a unit having the formula:



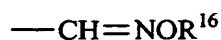
15 wherein R^4 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^5 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^4 and R^5 can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

- xviii) a unit having the formula:



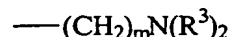
20 wherein R^6 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^7 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^6 and R^7 can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

- 25 xix) $-\text{NHOR}^{16}$, wherein R^{16} is hydrogen; $\text{C}_1\text{-C}_{12}$ linear or branched alkyl; acyl having the formula $-\text{COR}^{17}$, wherein R^{17} is $\text{C}_1\text{-C}_4$ alkyl; or mixtures thereof;
- xx) a unit having the formula:



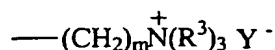
30 wherein R^{16} is hydrogen; $\text{C}_1\text{-C}_{12}$ linear or branched alkyl; $\text{C}_7\text{-C}_{22}$ linear or branched alkylenearyl; acyl having the formula $-\text{COR}^{17}$, R^{17} is $\text{C}_1\text{-C}_4$ alkyl; or mixtures thereof;

xxi) an amino unit having the formula:



wherein each R^3 is independently C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl; m is from 0 to 10;

5 xxii) a quaternary ammonium unit having the formula:



wherein each R^3 is independently C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl; Y is an anion of sufficient charge to provide electronic neutrality; m is from 0 to 10;

10 o) two R units on the same carbon atom can be taken together to form a carbonyl unit or carbonyl unit equivalent; and

p) mixtures thereof;

L is a linking group; R' is R or a unit which serves to irreversibly bind said saccharin enzyme inhibitor component to a target enzyme, [Poly] is a polymeric unit, i indicates the number of said saccharin units which comprise said conjugate and has the value of from 1 to 100; z is 0 or 1.

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3. A compound according to Claim 2 wherein R is:

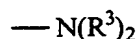
- 20 a) hydrogen;
- b) C_1 - C_8 linear unsubstituted alkyl;
- c) C_6 - C_{10} unsubstituted cycloalkyl;
- d) C_{10} and C_{15} branched alkenyl;
- e) aryl units selected from the group consisting of phenyl, naphthyl, 4-methoxyphenyl, 4-nitrophenyl, 4- $(\text{C}_1$ - C_4 alkyl)phenyl, and mixtures thereof;
- 25 f) C_4 - C_6 substituted or unsubstituted heterocyclic alkyl;
- g) C_3 - C_{18} substituted or unsubstituted heterocyclic alkenyl;
- h) alkylenearyl having the formula:



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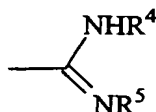
wherein R^2 is selected from the group consisting of phenyl, substituted phenyl, pyridinyl, substituted pyridinyl, and mixtures thereof;

i) an amino unit having the formula:



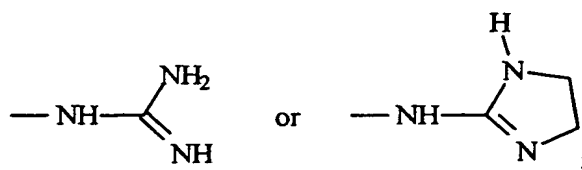
wherein each R^3 is independently hydrogen, methyl, ethyl, 2-hydroxyethyl, cyclopropyl, or mixtures thereof;

j) a unit having the formula:

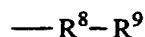


5 wherein R^4 and R^5 are each hydrogen, or R^4 and R^5 is taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

k) a unit having the formula:

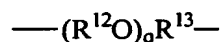


l) a unit having the formula:



wherein R^8 is:

- i) $\text{—(CH}_2\text{)}_p\text{—}$, wherein p is from 0 to 12;
- ii) —C(O)— ;
- iii) $\text{—NR}^{10}\text{—}$, wherein R^{10} is hydrogen, $\text{C}_1\text{—C}_4$ alkyl, or mixtures thereof;
- iv) —O— ;
- v) alkyleneoxyalkylene having the formula:



wherein R^{12} is $\text{C}_2\text{—C}_6$ linear or branched alkylene, substituted or unsubstituted phenylene; R^{13} is $\text{—(CH}_2\text{)}_p\text{—}$, wherein p is from 0 to 12; q is from 1 to 4;

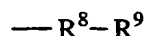
- vi) —S— ;
- vii) or mixtures thereof;

R^9 is:

- i) an alkyl unit selected from methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl;
- ii) a cycloalkyl unit selected from cyclopentyl, cyclohexyl, 4-methylcyclohexyl, 2,5-dimethylcyclopentyl;
- iii) an aryl unit selected from phenyl, 4-methoxyphenyl, 4-nitrophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,5-dichlorophenyl, 4-aminobenzyl, 4-guanidiobenzyl;

- iv) a heterocyclic unit selected from N-aziridinyl, 2-pyrrolindinyl, 3-pyrrolidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl;
- v) -OH, when the index p is from 1 to 4;
- vi) -SO₃M when the index p is from 1 to 4;
- 5 vii) -OSO₃M when the index p is from 2 to 4;
- viii) -NO₂;
- ix) chlorine, bromine, or mixtures thereof;
- x) -CF₃;
- xi) -COR¹⁴, wherein R¹⁴ is -OH, -NH₂, -N(CH₃)₂, or mixtures thereof;
- 10 xii) -NHOR¹⁶, wherein R¹⁶ is hydrogen; C₁-C₁₂ linear or branched alkyl; acyl having the formula -COR¹⁷, wherein R¹⁷ is C₁-C₄ alkyl; or mixtures thereof;
- xiii) a unit having the formula:
- $$\text{---CH=NO}R^{16}$$
- 15 wherein R¹⁶ is hydrogen or methyl; and
- m) mixtures thereof.

4. A compound according to either of Claims 2 or 3 wherein R is:
- a) hydrogen;
- 20 b) an alkyl unit selected from the group consisting of methyl, ethyl, propyl, isopropyl, n-butyl, t-butyl, n-pentyl, isopentyl, n-hexyl, 2-methyl hexyl, 2-ethyl, hexyl, and mixtures thereof;
- c) a cycloalkyl selected from the group consisting of cyclohexyl, 4-methylcyclohexyl, 4-isopropylcyclohexyl, and mixtures thereof;
- 25 d) a heterocyclic alkyl selected from the group consisting of 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyrrolindinyl, 3-pyrrolidinyl, 2-piperazinyl, N-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, N-morpholinyl, and mixtures thereof;
- e) an amino unit selected from the group consisting of methylamino, dimethylamino, ethylamino, diethylamino, dicyclopropyl, and mixtures thereof;
- 30 f) a heterocycle selected from the group consisting of amidine, 2-pyridinyl, pyrimidinyl, imidazolyl, and mixtures thereof;
- g) a unit having the formula:

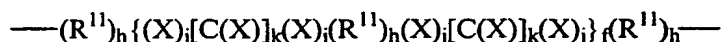


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wherein R^8 is -O- and R^9 is selected from the group consisting of methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, and mixtures thereof; and

h) mixtures thereof.

- 5 5. A compound according to any of Claims 2-4 wherein L has the formula:



wherein R^{11} is C_1 - C_{12} substituted or unsubstituted alkylene; C_2 - C_{12} substituted or unsubstituted alkenylene; substituted or unsubstituted C_3 - C_{12} cycloalkylene;

10 substituted or unsubstituted aromatic; substituted or unsubstituted heterocyclic; X is oxygen, sulfur, NR^{10} wherein R^{10} is hydrogen, C_1 - C_4 alkyl, phenyl, or R^{10} can be taken as part of a ring bonded to another moiety in the linking group, the indices h, j, and k are each independently 0 or 1, f is from 0 to 10.

- 15 6. A compound according to any of Claims 2-5 wherein said linking unit L is selected from the group consisting of:

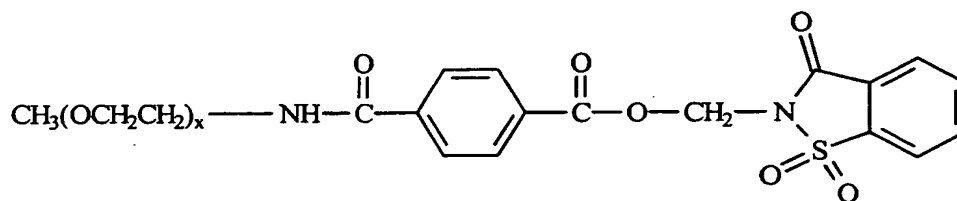
- i) $-(CH_2)_p-$, wherein p is from 0 to 12;
- ii) $-C(O)-$;
- 20 iii) $-C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- iv) $-C(X)R^{11}C(X)-$, wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- v) $-C(X)NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 25 vi) $-C(X)NR^{10}R^{11}NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- vii) $-NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 30 viii) $-NR^{10}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- ix) $-NR^{10}C(X)R^{11}NR^{10}-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 35

- x) $-\text{NR}^{10}\text{R}^{11}\text{C}(\text{X})\text{NR}^{10}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 5 xi) $-\text{NR}^{10}\text{C}(\text{X})\text{R}^{11}\text{C}(\text{X})\text{O}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xii) $-\text{OC}(\text{X})\text{R}^{11}\text{C}(\text{X})\text{NR}^{10}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 10 xiii) $-\text{NR}^{10}\text{C}(\text{X})\text{NR}^{10}\text{R}^{11}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xiv) $-\text{R}^{11}\text{NR}^{10}\text{C}(\text{X})\text{NR}^{10}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 15 xv) $-\text{R}^{11}\text{NR}^{10}\text{C}(\text{X})\text{NR}^{10}\text{R}^{11}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xvi) $-\text{NR}^{10}-$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof;
- 20 xvii) $-\text{O}-$;
- xviii) $-(\text{R}^{11})_t\text{C}(\text{X})(\text{R}^{11})_{t-}$; wherein R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1; wherein X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xix) $-(\text{R}^{11})_t\text{OC}(\text{O})(\text{R}^{11})_{t-}$; wherein R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- 25 xx) $-(\text{R}^{11})_t\text{C}(\text{O})\text{O}(\text{R}^{11})_{t-}$; wherein R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxi) $-(\text{R}^{11})_t\text{OC}(\text{O})\text{O}(\text{R}^{11})_{t-}$; wherein t is 0 or 1;
- xxii) alkyleneoxyalkylene having the formula:
- 30
$$\text{---}(\text{R}^{12}\text{O})_q\text{R}^{13}\text{---}$$
- wherein R^{12} is $\text{C}_2\text{-C}_6$ linear or branched alkylene, substituted or unsubstituted phenylene; R^{13} is $-(\text{CH}_2)_p-$, wherein p is from 0 to 12; q is 1 or 2;
- xxiii) $-\text{S}-$;

- xxiv) $-(R^{11})_tS(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxv) $-(R^{11})_tS(O)(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- 5 xxvi) $-(R^{11})_tSO_2(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxvii) or mixtures thereof.

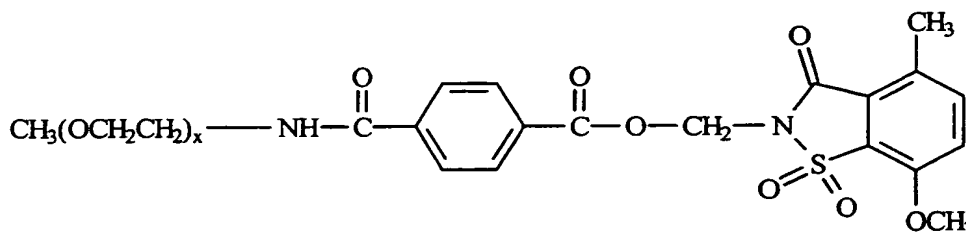
7. A compound according to any of Claims 2-6 wherein said [Poly] unit has a
10 molecular weight of from 1000 daltons to 8,000 daltons.

8. A compound according to Claim 2 having the formula:



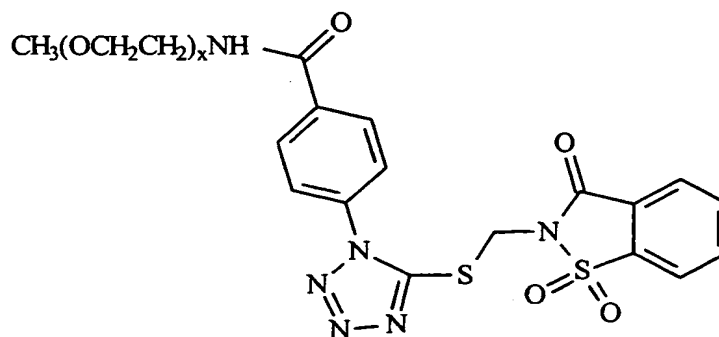
- 15 wherein x is from 50 to 250.

9. A compound according to Claim 2 having the formula:



- 20 wherein x has a value such that the [Poly] unit has a molecular weight of 5000 daltons.

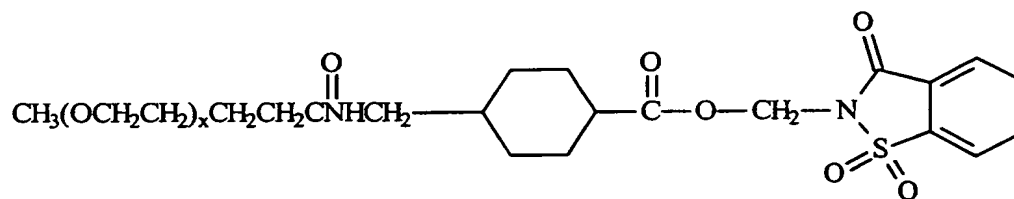
10. A compound according to Claim 2 having the formula:



wherein x is from 50 to 250.

11. A compound according to Claim 2 having the formula:

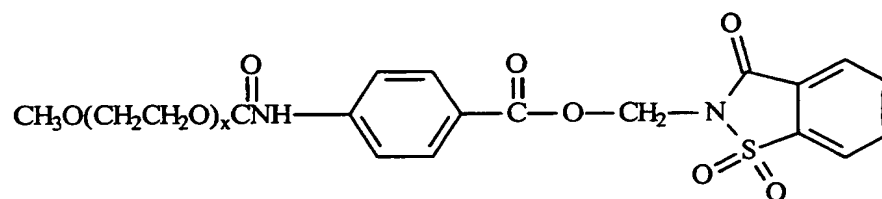
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wherein x is from 50 to 250.

12. A compound according to Claim 2 having the formula:

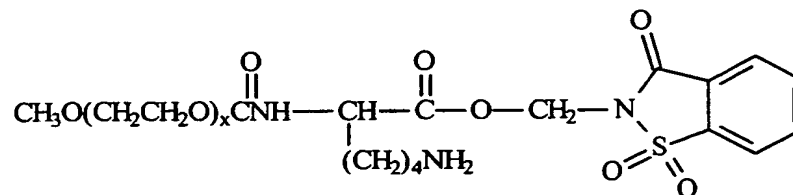
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wherein x is from 50 to 250.

13. A compound according to Claim 2 having the formula:

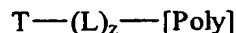
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wherein x is from 50 to 250.

14. A composition for inhibiting enzymes comprising:

- a) from 0.01% by weight, of one or more polymer conjugates having the formula:

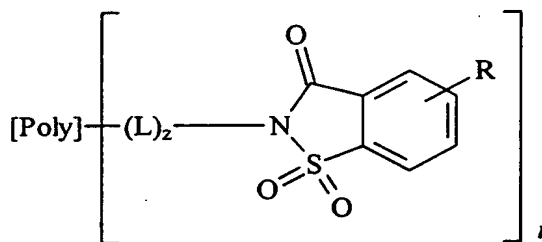


5 wherein T is a saccharin ring-comprising enzyme inhibitor component, L is a linking unit, [Poly] is a polymer component, z is 0 or 1; and

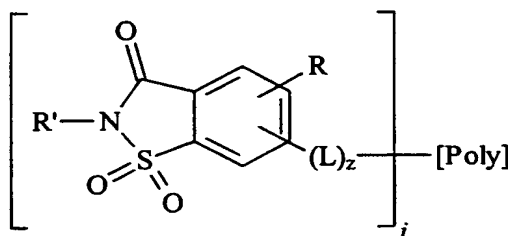
- b) the balance carriers and adjunct ingredients.

15. A composition according to Claim 14 having a saccharin inhibitor component of the formula:

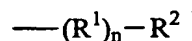
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or the formula:



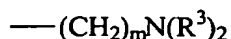
- a) hydrogen;
 b) C₁-C₁₈ substituted or unsubstituted, linear or branched alkyl;
 c) C₃-C₁₈ substituted or unsubstituted, linear or branched cycloalkyl
 d) C₂-C₁₈ substituted or unsubstituted, linear or branched alkenyl;
 e) C₂-C₁₈ substituted or unsubstituted, linear or branched alkynyl;
 f) C₆-C₁₈ substituted or unsubstituted aryl;
 g) C₂-C₁₈ substituted or unsubstituted heterocyclic alkyl;
 h) C₃-C₁₈ substituted or unsubstituted heterocyclic alkenyl;
 i) alkylenearyl having the formula:



wherein R¹ is C₁-C₁₂ linear or branched alkylene, C₂-C₁₂ linear or branched alkenylene, or mixtures thereof; R² C₆-C₁₈ substituted or unsubstituted aryl, or mixtures thereof; n is from 1 to 16;

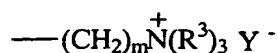
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- j) an amino unit having the formula:



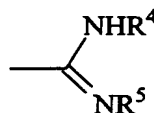
wherein each R^3 is independently $\text{C}_1\text{-C}_{18}$ substituted or unsubstituted, linear or branched alkyl; m is from 0 to 10;

- 5 k) a quaternary ammonium unit having the formula:



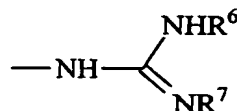
wherein each R^3 is independently $\text{C}_1\text{-C}_{18}$ substituted or unsubstituted, linear or branched alkyl; Y is an anion of sufficient charge to provide electronic neutrality; m is from 0 to 10;

- 10 l) a unit having the formula:



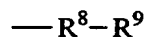
wherein R^4 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^5 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^4 and R^5 can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

- 15 m) a unit having the formula:



wherein R^6 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^7 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; R^6 and R^7 can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;

- 20 n) a unit having the formula:



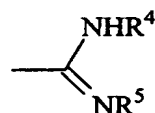
wherein R^8 is:

- i) $\text{---}(\text{CH}_2)_p\text{---}$, wherein p is from 0 to 12;
 ii) ---C(O)--- ;
 25 iii) $\text{---C(X)NR}^{10}\text{---}$, wherein R^{10} is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
 iv) $\text{---C(X)R}^{11}\text{C(X)---}$, wherein R^{11} is $\text{C}_1\text{-C}_{12}$ alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;

- v) $-C(X)NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- vi) $-C(X)NR^{10}R^{11}NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- vii) $-NR^{10}C(X)-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- viii) $-NR^{10}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- ix) $-NR^{10}C(X)R^{11}NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- x) $-NR^{10}R^{11}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xi) $-NR^{10}C(X)R^{11}C(X)O-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xii) $-OC(X)R^{11}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xiii) $-NR^{10}C(X)NR^{10}R^{11}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- xiv) $-R^{11}NR^{10}C(X)NR^{10}-$, wherein R^{10} is hydrogen, C_1-C_4 alkyl, or mixtures thereof; R^{11} is C_1-C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; wherein X is oxygen, sulfur, NR^{10} , and mixtures thereof;

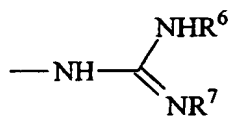
- xv) $-R^{11}NR^{10}C(X)NR^{10}R^{11}-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof; R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 5 xvi) $-NR^{10}-$, wherein R^{10} is hydrogen, C_1 - C_4 alkyl, or mixtures thereof;
- xvii) $-O-$;
- xviii) $-(R^{11})_tC(X)(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1; X is oxygen, sulfur, NR^{10} , and mixtures thereof;
- 10 xix) $-(R^{11})_tOC(O)(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xx) $-(R^{11})_tC(O)O(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxi) alkyleneoxyalkylene having the formula:
- 15
$$-(R^{12}O)_qR^{13}-$$
- wherein R^{12} is C_2 - C_6 linear or branched alkylene, substituted or unsubstituted phenylene; R^{13} is $-(CH_2)_p-$, wherein p is from 0 to 12; q is from 1 to 4;
- xxii) $-S-$;
- 20 xxiii) $-(R^{11})_tS(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxiv) $-(R^{11})_tS(O)(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- xxv) $-(R^{11})_tSO_2(R^{11})_{t-}$; wherein R^{11} is C_1 - C_{12} alkylene, substituted or unsubstituted phenylene, or mixtures thereof; t is 0 or 1;
- 25 xxvi) or mixtures thereof;
- R^9 is:
- i) hydrogen;
- ii) C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl;
- 30 iii) C_3 - C_{18} substituted or unsubstituted, linear or branched cycloalkyl;
- iv) C_2 - C_{18} substituted or unsubstituted, linear or branched alkenyl;
- v) C_2 - C_{18} substituted or unsubstituted, linear or branched alkynyl;
- vi) C_6 - C_{18} substituted or unsubstituted aryl;
- vii) C_2 - C_{18} substituted or unsubstituted heterocyclic alkyl;
- 35 viii) C_3 - C_{18} substituted or unsubstituted heterocyclic alkenyl;

- ix) -OH;
 x) -SO₃M;
 xi) -OSO₃M;
 xii) -NO₂;
 5 xiii) halogen selected from fluorine, chlorine, bromine, iodine, or mixtures thereof;
 xiv) -C(Hal)₃, wherein each Hal is fluorine, chlorine, bromine, iodine, or mixtures thereof;
 xv) -COR¹⁴; wherein R¹⁴ is hydrogen, -OH, C₁-C₁₂ alkyl, C₁-C₁₂ alkoxy, or mixtures thereof; -N(R¹⁵)₂, or mixtures thereof; each R¹⁵ is independently hydrogen, -OH, C₁-C₄ alkyl, or mixtures thereof;
 10 xvi) -CH(OR¹⁴)₂ wherein R¹⁴ is hydrogen, C₁-C₁₂ alkyl, or two R¹⁴ units can be taken together to form a ring having from 3 to 5 carbon atoms; or mixtures thereof;
 15 xvii) a unit having the formula:



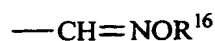
wherein R⁴ is hydrogen, C₁-C₄ alkyl, or mixtures thereof; R⁵ is hydrogen, C₁-C₄ alkyl, or mixtures thereof; R⁴ and R⁵ can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;
 20

- xviii) a unit having the formula:



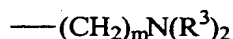
wherein R⁶ is hydrogen, C₁-C₄ alkyl, or mixtures thereof; R⁷ is hydrogen, C₁-C₄ alkyl, or mixtures thereof; R⁶ and R⁷ can be taken together to form a heterocyclic ring comprising from 3 to 5 carbon atoms;
 25

- xix) -NHOR¹⁶, wherein R¹⁶ is hydrogen; C₁-C₁₂ linear or branched alkyl; acyl having the formula -COR¹⁷, wherein R¹⁷ is C₁-C₄ alkyl; or mixtures thereof;
 30 xx) a unit having the formula:



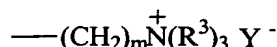
wherein R^{16} is hydrogen; C_1 - C_{12} linear or branched alkyl; C_7 - C_{22} linear or branched alkylenearyl; acyl having the formula $-COR^{17}$, R^{17} is C_1 - C_4 alkyl; or mixtures thereof;

xxi) an amino unit having the formula:



wherein each R^3 is independently C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl; m is from 0 to 10;

xxii) a quaternary ammonium unit having the formula:



wherein each R^3 is independently C_1 - C_{18} substituted or unsubstituted, linear or branched alkyl; Y is an anion of sufficient charge to provide electronic neutrality; m is from 0 to 10;

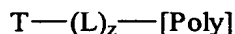
o) two R units on the same carbon atom can be taken together to form a carbonyl unit or carbonyl unit equivalent; and

p) mixtures thereof;

L is a linking group; R' is R or a unit which serves to irreversibly bind said saccharin enzyme inhibitor component to a target enzyme, $[Poly]$ is a polymeric unit, i indicates the number of said saccharin units which comprise said conjugate and has the value of from 1 to 100; z is 0 or 1.

16. A composition for application to human skin, said composition comprising:

a) from 0.01% by weight, of one or more polymer conjugates unit which are capable of inhibiting one or more proteolytic enzymes having the formula:



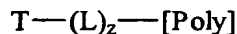
wherein T is a saccharin ring-comprising enzyme inhibitor component, L is a linking unit, $[Poly]$ is a polymer component, z is 0 or 1;

b) from 0.01% by weight, of an adjunct biologically active ingredient; and

c) the balance carriers and adjunct ingredients.

17. A method for preventing human skin irritation, said method comprising the step of contacting human skin with a composition comprising:

- a) from 0.01% by weight, of one or more polymer conjugates capable of inhibiting one or more proteolytic enzymes having the formula:



5 wherein T is a saccharin ring-comprising enzyme inhibitor component, L is a linking unit, [Poly] is a polymer component, z is 0 or 1; and

- b) the balance carriers and adjunct ingredients.

18. A method according to either Claim 16 or 17 wherein said adjunct ingredients are
10 selected from the group consisting of petroleum-based emollients, sucrose ester fatty acids, polyethylene glycol and derivatives thereof, humectants, fatty acid esters, alkyl ethoxylates, fatty acid ester ethoxylates, fatty alcohols, polysiloxanes, propylene glycol and derivatives thereof, glycerin, glyceride, acetoglycerides, and
15 ethoxylated glycerides of C₁₂-C₂₂ fatty acids, triethylene glycol and derivatives thereof, waxes, fatty acids, fatty alcohol ethers, propoxylated fatty alcohols, fatty esters of polyhydroxy alcohols, lanolin, kaolin, and mixtures thereof.